REMARKS

Claims 1-36 were pending. Claims 2, 3, 5, 19-22, and 34-36 are withdrawn from consideration. Claim 23 is amended and new claim 37 has been added. Support for the amendments and new claim can be found in the claims as originally filed. In particular, support for claim 37 can be found on page 46, lines 1-10. No new matter has been added. Accordingly, claims 1-37 will be pending upon entry of the amendment and new claim.

Rejections Under 35 U.S.C. § 103

Claims 1, 4, 6-18, and 22-33 are rejected under 35 U.S.C. § 103 as being unpatentable over Maciaszek et al. (Journal of Virology, 1998, Vol. 72, No. 7, pp. 5862-69) in view of Gander et al. (U.S. 4,323, 581).

The Examiner asserts that Maciaszek et al. teach that retinoid-induced repression of HIV core promoter activity inhibits virus replication, that retinoid inhibits the infection of cells, and that retinol or its metabolite represses HIV-1 replication.

The Examiner admits that Maciaszek et al. do not teach the use of 4-HPR. However, the Examiner states that Gander et al. teach that 4-HPR is a retinoid derivative, having the same function as retinoids, but with low toxicity. The Examiner concludes that it would have been obvious to use 4-HPR for the treatment or for inhibiting HIV infection of cells.

Applicants submit that a *prima facie* case of obviousness has not been established. Withdrawal of the rejection is requested. To establish *prima facie* obviousness of a claimed invention, all of the claimed elements must be taught or suggested by the prior art. M.P.E.P. § 2143.03. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. KSR International Co. v. Teleflex Inc., 550 U.S. 398, 82 USPQ 1385, 1396 (2007).

Maciaszek et al. do not teach that retinoid induces repression of HIV core promoter activity, HIV infection, and HIV replication in all cells. At best, Maciaszek et al. teach that addition of retinoid during macrophage differentiation results in MDMs that are nonpermissive for HIV-1 replication.

> Addition of physiological concentrations of retinoids, either retinol or retinoic acid, during differentiation results in MDMs that are nonpermissive for HIV-1 replication. However, retinoid treatment after this critical period has no effect on virus replication. (See Maciaszek et al. at page 5866, second full paragraph in the second column)

Maciaszek et al. teach that treatment of macrophages after differentiation has no effect. Furthermore, Maciaszek et al. only discuss effects at physiological concentrations of retinoid and cites studies showing higher doses of vitamin A (>20,000 IU/day) increased the risk of AIDS mortality (Maciaszek et al. at page 5862, second column). Moreover, Maciaszek et al. cite to the conflicting nature of the data surrounding the role of retinoids. For example Maciaszek et al. note that others had shown that RA treatment stimulates HIV-1 replication in acutely infected U937 cells and that in some studies the effects of RA were donor dependent (Maciaszek et al. at page 5863, first column). Given the conflicting nature of the data, a person of skill in the art would not have a reasonable expectation of success in inhibiting HIV infection with a ceramide-generating retinoid based on Maciaszek et al.

Maciaszek et al. specifically teach that retinoids inhibit HIV only in macrophages and only if given during macrophage differentiation. Accordingly, Maciaszek et al. either individually or in combination with Gander do not render the claims obvious. Further, Applicants have added new claim 37 directed to the inhibition of HIV-1 infection of differentiated macrophages. Maciaszek et al. does not teach or suggest the method of claim 27; indeed, Maciaszek et al. specifically teaches away from this claim.

Moreover, Maciaszek et al. do not teach or suggest that ceramide-generating retinoid would inhibit viral entry or exit. Regarding claim 23, the Examiner alleges that the preamble of the claim is not a limitation. Applicants disagree. Nevertheless, without acquiescing to the basis of the rejection and solely to facilitate prosecution, Applicants have amended claim 23. As amended, claim 23 is directed to:

> A method of inhibiting a viral attachment/entry or exit phase of a virus by administering a pharmaceutical composition to a cell susceptible to infection by a virus, wherein the pharmaceutical composition comprises an inhibitor of at least one enzyme essential to ceramide metabolism, thereby inhibiting viral attachment/entry or exit phase of the virus.

As amended, claim 23 requires that the inhibition of at least one enzyme essential to ceramide metabolism results in inhibition of viral attachment/entry or exit of the virus. Maciaszek et al. does not teach or suggest inhibition of viral entry or exit and Gander does not cure the deficiency.

As the Examiner admits, Maciaszek et al. do not teach or suggest 4-HPR. But the Examiner relies on Gander to cure this deficiency. In doing so, the Examiner states that Gander teaches 4-HPR has the "same function" as retinoid. This is incorrect. At best, Gander teaches that 4-HPR has the same anti-cancer activities as retinoids. Nowhere does Gardner teach or suggest that 4-HPR can act as a functional substitution for retinoids for all biological functions. Accordingly, one of skill in the art would not have been motivated to use the 4-HPR taught by Gander to inhibit the expression and replication of HIV virus in undifferentiated macrophages as taught by Maciaszek et al.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Dated: May 5, 2011

Respectfully submitted,

Electronic signature:
/Andrew W. Shyjan, Ph.D., Esq./
Andrew W. Shyjan, Ph.D., Esq.
Registration No.: 61,294
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5558
Attorneys/Agents For Applicant